

1 WHAT IS CLAIMED IS:

2
3 ~~1. A method of establishing a patient-specific optimally effective dose for administration of~~
4 ~~a radiopharmaceutical to a patient, the method comprising:~~

5 ~~determining a maximum tolerated dose for the radiopharmaceutical for the patient~~
6 ~~population;~~

7 ~~determining a desired total body dose of the radiopharmaceutical for the patient;~~

8 ~~determining the clearance profile for the radiopharmaceutical or a radiopharmaceutical~~
9 ~~analog;~~

10 ~~determining the patient's mass and maximum effective mass;~~

11 ~~selecting the lower of the patient's mass and maximum effective mass;~~

12 ~~determining the activity hours for the radiopharmaceutical or radiopharmaceutical analog~~
13 ~~based on the lower of the patient's mass or maximum effective mass and the desired total body~~
14 ~~dose;~~

15 ~~administering a tracer dose of the radiopharmaceutical or the radiopharmaceutical analog~~
16 ~~to the patient;~~

17 ~~determining the residence time for the radiopharmaceutical or the radiopharmaceutical~~
18 ~~analog; and~~

19 ~~establishing the optimally effective dose of the radiopharmaceutical for the patient by~~
20 ~~solving for therapeutic dose in the following equation:~~

21
22
$$\text{therapeutic dose} = \frac{\text{Activity Hours}}{\text{Residence time}} \times \frac{\text{desired total body dose}}{\text{maximum tolerated dose.}}$$

23

24
25 2. ~~The method of claim 1, wherein the step of determining the maximum tolerated dose~~
26 ~~comprises performing a dose escalation study for the radiopharmaceutical in a patient~~
27 ~~population.~~

28
29 3. ~~The method of claim 1, wherein the maximum effective mass is based on the~~
30 ~~radiopharmaceutical.~~
31

SUB B22
1 4. The method of claim 1, wherein the maximum effective mass is correlated to the lean
body mass of the patient.

3
4 5. The method of claim 1, wherein the maximum effective mass is based on the gender and
5 height of the patient.

6
7 6. The method of claim 1, wherein the step of determining the clearance profile comprises
8 performing a study following measurement over time of the loss of radioactivity from an
9 administered radiopharmaceutical.

10
11 7. The method of claim 1, wherein the step of determining the clearance profile comprises
12 performing a dose escalation study for the radiopharmaceutical.

13
14 8. The method of claim 1, wherein the clearance profile provides an activity-time curve
15 shape for the radiopharmaceutical.

16
17 9. The method of claim 1, wherein the clearance profile provides an indication of the
18 number of exponential terms in the function defining the pattern of clearance for the
19 radiopharmaceutical.

20
21 10. The method of claim 1, wherein the step of determining the residence time for the
22 radiopharmaceutical comprises:
23 making measurements of radioactivity in the whole body of the patient at each of a
24 number of time points,
25 calculating percent injected activity of the radiopharmaceutical at each of the time points,
26 and
27 establishing the residence time by plotting the time points vs. percent injected activity on
28 a semilog graph and determining 37% injected activity.

29
30 11. The method of claim 10, wherein each time point is background corrected.
31

12. The method of claim 10, wherein the number of time points are correlated to the clearance profile of the radiopharmaceutical so that at least 2 measurements are made if the radiopharmaceutical has monoexponential clearance, at least 4 measurements are made if the radiopharmaceutical has biexponential clearance, and at least 6 measurements are made if the radiopharmaceutical has triexponential clearance.

13. The method of claim 1, wherein the step of determining the residence time for the radiopharmaceutical comprises:

making measurements of radioactivity in the whole body of the patient at each of three time points and solving in the following equation:

Sub 1

$$\text{Residence time (hr)} = \frac{t_2 (1 - \frac{c_2}{c_1})}{\log_e (\frac{c_1}{c_2})} + \frac{\frac{c_2}{c_1} (t_3 - t_2)}{\log_e (\frac{c_2}{c_3})}$$

where t_1 , t_2 , and t_3 are the three time points and c_1 , c_2 , and c_3 are the counts at each of the t_1 , t_2 , and t_3 time points.

14. The method of claim 13, wherein each time point is background corrected.

15. The method of claim 1, wherein the step of determining the residence time for the radiopharmaceutical comprises:

making measurements of radioactivity in the whole body of the patient at each of a number of time points, and solving for τ in the following equation:

$$\tau = \frac{\sum_{i=1}^n \frac{a_i}{\alpha_i}}{\sum_{i=1}^n a_i}$$

where τ is residence time, n is the number of exponential terms as determined by the clearance profile, a_i are the intercepts, and α_i are the slopes of the i th exponential term.

16. The method of claim 15, wherein each time point is background corrected.

1
2 17. The method of claim 15, wherein the number of time points are correlated to the
3 clearance profile of the radiopharmaceutical so that at least 2 measurements are made if the
4 radiopharmaceutical has monoexponential clearance, at least 4 measurements are made if the
5 radiopharmaceutical has biexponential clearance, and at least 6 measurements are made if the
6 radiopharmaceutical has triexponential clearance.

7
8 18. The method of claim 1, wherein the step of determining the residence time for the
9 radiopharmaceutical comprises:

10 making measurements of radioactivity in the whole body of the patient at each of a
11 number of time points, generating an activity-time curve, and using the trapezoidal rule or
12 Simpson's rule.

13
14 19. An optimally effective therapeutic dose of a radiopharmaceutical for administration to a
15 patient, said optimally effective therapeutic dose determined by the method comprising:

16 determining a maximum tolerated dose for the radiopharmaceutical for the patient
17 population;

18 determining a desired total body dose of the radiopharmaceutical for the patient;

19 determining the clearance profile for the radiopharmaceutical or a radiopharmaceutical
20 analog;

21 determining the patient's mass and maximum effective mass;

22 selecting the lower of the patient's mass and maximum effective mass;

23 determining the activity hours for the radiopharmaceutical or radiopharmaceutical analog
24 based on the lower of the patient's mass or maximum effective mass and the desired total body
25 dose;

26 administering a tracer dose of the radiopharmaceutical or the radiopharmaceutical analog
27 to the patient;

28 determining the residence time for the radiopharmaceutical or the radiopharmaceutical
29 analog; and

30 establishing the optimally effective dose of the radiopharmaceutical for the patient by
31 solving for therapeutic dose in the following equation:

therapeutic dose = $\frac{\text{Activity Hours}}{\text{Residence time}} \times \frac{\text{desired total body dose}}{\text{maximum tolerated dose}}$.

20. A method of establishing a patient-specific optimally effective dose for administration of a radiopharmaceutical to a patient, the method comprising:

determining the desired total body dose (TBD) of the radiopharmaceutical for the patient;

determining the patient's mass (M) and maximum effective mass (MEM);

selecting the lower of the patient's mass and maximum effective mass (M or MEM);

determining the activity hours (AH) for the radiopharmaceutical or a radiopharmaceutical analog by reference to Equation I:

Sub B467

$$AH = \frac{TBD \times (M \text{ or } MEM)}{\left[\sum_{elec} \Delta_{elec} + \sum_{phot} \Delta_{phot} \phi_{phot}^{TB} \right]}$$

(Equation I)

where

$$\left[\sum_{elec} \Delta_{elec} + \sum_{phot} \Delta_{phot} \phi_{phot}^{TB} \right]$$

in Equation 1 represents the sum of electron energy and photon energy deposited in the total body of the patient by the radiopharmaceutical or radiopharmaceutical analog;

determining the patient-specific residence time of an administered tracer dose of the radiopharmaceutical or the radiopharmaceutical analog in the whole body of the patient; and

establishing a therapeutic dose of the radiopharmaceutical for the patient by dividing the activity hours by the patient-specific residence time to obtain a value and optionally multiplying the value by an attenuation factor, said attenuation factor being determined by the TBD divided by the maximum tolerated dose for the radiopharmaceutical.

21. The method of claim 20 further comprising the step of determining the clearance profile for the radiopharmaceutical or the radiopharmaceutical analog, said clearance profile providing a

1 minimum number of time points for determination of the residence time of the
2 radiopharmaceutical or the radiopharmaceutical analog.

3
4 22. The method of claim 20, wherein the step of determining the residence time for the
5 radiopharmaceutical comprises:

6 making measurements of radioactivity in the whole body of the patient at each of a
7 number of time points, and solving for τ in the following equation:

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9
10
11
12

$$\tau = \frac{\sum_{i=1}^n \frac{a_i}{\alpha_i}}{\sum_{i=1}^n a_i}$$

13 where τ is residence time, n is the number of exponential terms as determined by
14 the clearance profile, a_i are the intercepts, and α_i are the slopes of the i th exponential
15 term.
16
17
18
19

20
21 23. The method of claim 22, wherein each time point is background corrected.

22
23 24. The method of claim 22, wherein the number of time points are correlated to the
24 clearance profile of the radiopharmaceutical so that at least 2 measurements are made if the
25 radiopharmaceutical has monoexponential clearance, at least 4 measurements are made if the
26 radiopharmaceutical has biexponential clearance, and at least 6 measurements are made if the
27 radiopharmaceutical has triexponential clearance.
28

29
30 25. A method of establishing a patient-specific optimally effective dose for administration of
31 a radiopharmaceutical to a patient, the method comprising:

32 determining a maximum tolerated dose for the radiopharmaceutical for the patient
33 population;

34 determining a desired total body dose of the radiopharmaceutical for the patient;

35 determining the clearance profile for the radiopharmaceutical or a radiopharmaceutical
36 analog;

37 determining a lean body mass for the patient;

1 determining the activity hours for the radiopharmaceutical or radiopharmaceutical analog
2 based on the patient's lean body mass and the desired total body dose;
3 administering a tracer dose of the radiopharmaceutical or the radiopharmaceutical analog
4 to the patient;
5 determining the residence time for the radiopharmaceutical or the radiopharmaceutical
6 analog; and
7 establishing the optimally effective dose of the radiopharmaceutical for the patient by
8 solving for therapeutic dose in the following equation:

$$\text{therapeutic dose} = \frac{\text{Activity Hours}}{\text{Residence time}} \times \frac{\text{desired total body dose}}{\text{maximum tolerated dose.}}$$

12
13 26. The method of claim 25, wherein the step of determining the residence time for the
14 radiopharmaceutical comprises:

15 making measurements of radioactivity in the whole body of the patient at each of a
16 number of time points, and solving for τ in the following equation:

$$\tau = \frac{\sum_{i=1}^n \frac{a_i}{\alpha_i}}{\sum_{i=1}^n a_i}$$

18 where τ is residence time, n is the number of exponential terms as determined by
19 the clearance profile, a_i are the intercepts, and α_i are the slopes of the i th exponential
20 term.

21
22 27. An optimally effective therapeutic dose of a radiopharmaceutical for administration to a
23 patient, said optimally effective therapeutic dose determined by the method comprising:

24 determining a maximum tolerated dose for the radiopharmaceutical for the patient
25 population;

26 determining a desired total body dose of the radiopharmaceutical for the patient;

27 determining the clearance profile for the radiopharmaceutical or a radiopharmaceutical
28 analog;

1 determining a lean body mass for the patient;
2 determining the activity hours for the radiopharmaceutical or radiopharmaceutical analog
3 based on the patient's lean body mass and the desired total body dose;
4 administering a tracer dose of the radiopharmaceutical or the radiopharmaceutical analog
5 to the patient;
6 determining the residence time for the radiopharmaceutical or the radiopharmaceutical
7 analog; and
8 establishing the optimally effective dose of the radiopharmaceutical for the patient by
9 solving for therapeutic dose in the following equation:

$$\text{therapeutic dose} = \frac{\text{Activity Hours}}{\text{Residence time}} \times \frac{\text{desired total body dose}}{\text{maximum tolerated dose.}}$$

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14 28. The method of claim 27, wherein the step of determining the residence time for the
15 radiopharmaceutical comprises:

16 making measurements of radioactivity in the whole body of the patient at each of a
17 number of time points, and solving for τ in the following equation:

$$\tau = \frac{\sum_{i=1}^n \frac{a_i}{\alpha_i}}{\sum_{i=1}^n a_i}$$

18
19 where τ is residence time, n is the number of exponential terms as determined by
20 the clearance profile, a_i are the intercepts, and α_i are the slopes of the i th exponential
21 term.
22

23 29. A computer system including an input device, an output device and a central processing
24 unit, the computer system being programmed to determine a desired dose of a
25 radiopharmaceutical to be administered to a patient, the computer system in use:

26 receiving an input of at least one patient parameter:

27 from the at least one patient parameter, determining an activity hour parameter to provide
28 a maximum tolerated dose of the radiopharmaceutical ;

1 receiving an input of an initial activity count of a radiotracer;
2 receiving an input of at least one subsequent activity count of the radiotracer;
3 determining a residence time of the radiopharmaceutical from the initial activity count
4 and the at least one subsequent activity counts;
5 determining a patient specific dose of the radiopharmaceutical from the projected
6 residence time and the activity hour parameter; and
7 providing an output of the patient specific dose.
8
9

10 30. The computer system of claim 29, wherein the at least one patient parameter is one or
11 more parameters selected from the group consisting of patient mass, patient height and patient
12 gender.
13

14 31. The computer system of claim 30, wherein the at least one patient parameter includes the
15 patient mass, the computer system in use determining the activity hour parameter from the lesser
16 one of the patient mass and a maximum effective mass.
17

18 32. The computer system of claim 31, wherein the maximum effective mass is read from a
19 table of maximum effective mass versus patient height.
20

21 33. The computer system of claim 29, wherein the residence time is determined by
22 fitting a curve to the initial activity count and the at least one subsequent activity count;
23 and
24 solving the curve for the residence time.
25

26 34. The computer system of claim 33, wherein the curve is monoexponential.
27

28 35. The computer system of claim 33, wherein two subsequent activity counts are used when
29 fitting the curve.
30

31 36. The computer system of claim 33, wherein the curve is fitted using a numerical method.

1
2 37. The computer system of claim 36, wherein the numerical method is a least squares fit
3 method.

4
5 38. The computer system of claim 33, wherein,
6 after receiving an input of the first subsequent activity count, a preliminary patient
7 specific dose is determined; and
8 if the preliminary patient specific dose exceeds a vendor-provided dose, an output is
9 generated warning that an additional vendor-provided dose may be required.

10
11 39. The computer system of claim 31, wherein the maximum effective mass is determined
12 from a formula of maximum effective mass versus patient height.

13
14 40. The computer system of claim 29, wherein the activity hour parameter is read from a
15 database of activity hour parameters for particular maximum tolerated doses and particular
16 patient parameters.

17
18 41. The computer system of claim 29, wherein the initial and subsequent activity counts
19 received by the computer have been corrected to take into account of background radiation prior
20 to being received by the computer system

21
22 42. The computer system of claim 29, wherein the initial and subsequent activity counts
23 received by the computer are corrected to take into account of background radiation after being
24 received by the computer system.

25
26 43. The computer system of claim 42, wherein the correction to take account of background
27 radiation is performed by:
28 receiving an input of a background radiation count, and
29 subtracting the background radiation count from the appropriate activity count.
30

1 44. The computer system of claim 42, wherein the correction to take account of background
2 radiation is performed by:

3 receiving an input of a plurality of activity counts;

4 receiving an input of a plurality of related background radiation counts;

5 determining a plurality of intermediate corrected activity counts from the activity counts
6 and the related background radiation counts; and

7 determining a corrected activity count as a mean of the intermediate corrected activity
8 counts.

9
10 45. The computer system of claim 29, wherein doses for less tolerant patients is determined
11 by:

12 displaying categories of less tolerant patients;

13 receiving an input of the selection of a category into which a less tolerant patient falls;

14 and

15 setting a desired total body dose for the particular patient equal to the total body dose for
16 the selected category.

17
18 46. The computer system of claim 29 wherein patient-specific desired total body doses may
19 be specified by the user of the system.

20
21 47. A computer usable medium having computer readable program code embodied therein
22 for causing a computer to determine a desired dose of a radiopharmaceutical to be administered
23 to a patient, the computer readable program code causing the computer in use to:

24 receive an input of at least one patient parameter:

25 from the at least one patient parameter, determine an activity hour parameter to provide a
26 maximum tolerated dose of the radiopharmaceutical ;

27 receive an input of an initial activity count of a radiotracer;

28 receive an input of at least one subsequent activity count of the radiotracer;

29 determine a residence time of the radiopharmaceutical from the initial activity count and
30 the at least one subsequent activity counts;

1 determine a patient specific dose of the radiopharmaceutical from the projected residence
2 time and the activity hour parameter; and
3 provide an output of the patient specific dose.
4
5

6 48. The computer usable medium of claim 47, wherein the at least one patient parameter is
7 one or more parameters selected from the group consisting of patient mass, patient height and
8 patient gender.
9

10 49. The computer usable medium of claim 48, wherein the at least one patient parameter
11 includes the patient mass, the computer in use determining the activity hour parameter from the
12 lesser one of the patient mass and a maximum effective mass.
13

14 50. The computer usable medium of claim 49, wherein the maximum effective mass is read
15 in use by the computer from a table of maximum effective mass versus patient height.
16

17 51. The computer usable medium of claim 47, wherein the residence time is determined by
18 the computer in use by
19 fitting a curve to the initial activity count and the at least one subsequent activity count;
20 and
21 solving the curve for the residence time.
22

23 52. The computer usable medium of claim 51, wherein the curve is monoexponential.
24

25 53. The computer usable medium of claim 51, wherein two subsequent activity counts are
26 used when fitting the curve.
27

28 54. The computer usable medium of claim 51, wherein the curve is fitted using a numerical
29 method.
30

1 55. The computer usable medium of claim 54, wherein the numerical method is a least
2 squares fit method.

3
4 56. The computer usable medium of claim 51, wherein the computer readable program code
5 causes the computer in use to,

6 after receiving an input of the first subsequent activity count, determine a preliminary
7 patient specific dose; and

8 if the preliminary patient specific dose exceeds a vendor-provided dose, generate an
9 output warning that an additional vendor-provided dose may be required.

10
11 57. The computer usable medium of claim 49, wherein the maximum effective mass is
12 determined from a formula of maximum effective mass versus patient height.

13
14 58. The computer usable medium of claim 47, wherein the activity hour parameter is read in
15 use by the computer from a database of activity hour parameters for particular maximum
16 tolerated doses and particular patient parameters.

17
18 59. The computer usable medium of claim 47, wherein the initial and subsequent activity
19 counts received by the computer in use have been corrected to take into account of background
20 radiation prior to being received by the computer.

21
22 60. The computer usable medium of claim 47, wherein the initial and subsequent activity
23 counts received by the computer in use are corrected to take into account of background
24 radiation after being received by the computer.

25
26 61. The computer usable medium of claim 60, wherein the correction to take account of
27 background radiation is performed in use by the computer by:

28 receiving an input of a background radiation count; and

29 subtracting the background radiation count from the appropriate activity count.
30

62. The computer usable medium of claim 60, wherein the correction to take account of background radiation is performed in use by the computer by:

- receiving an input of a plurality of activity counts;
- receiving an input of a plurality of related background radiation counts;
- determining a plurality of intermediate corrected activity counts from the activity counts and the related background radiation counts; and
- determining a corrected activity count as a mean of the intermediate corrected activity counts.

63. The computer usable medium of claim 47, wherein doses for less tolerant patients is determined by the computer by:

- displaying categories of less tolerant patients;
- receiving an input of the selection of a category into which a less tolerant patient falls;
- and
- setting a desired total body dose for the particular patient equal to the total body dose for the selected category.

64. The computer usable medium of claim 47, wherein patient-specific desired total body doses may be specified in use by the user of the computer.

65. A data storage device readable by a machine, tangibly embodying a program of instructions executable by a machine to perform method steps to determine a desired dose of a radiopharmaceutical to be administered to a patient, the method steps comprising:

- receiving an input of at least one patient parameter:
- from the at least one patient parameter, determining an activity hour parameter to provide a maximum tolerated dose of the radiopharmaceutical ;
- receiving an input of an initial activity count of a radiotracer;
- receiving an input of at least one subsequent activity count of the radiotracer;
- determining a residence time of the radiopharmaceutical from the initial activity count and the at least one subsequent activity counts;

1 determining a patient specific dose of the radiopharmaceutical from the projected
2 residence time and the activity hour parameter; and
3 providing an output of the patient specific dose.
4

5 66. The data storage device of claim 65, wherein the at least one patient parameter is one or
6 more parameters selected from the group consisting of patient mass, patient height and patient
7 gender.
8

9 67. The data storage device of claim 66, wherein the at least one patient parameter includes
10 the patient mass, the machine in use determining the activity hour parameter from the lesser one
11 of the patient mass and a maximum effective mass.
12

13 68. The data storage device of claim 67, wherein the maximum effective mass is read from a
14 table of maximum effective mass versus patient height.
15

16 69. The data storage device of claim 65, wherein the residence time is determined by
17 fitting a curve to the initial activity count and the at least one subsequent activity count;
18 and
19 solving the curve for the residence time.
20

21 70. The data storage device of claim 69, wherein the curve is monoexponential.
22

23 71. The data storage device of claim 69, wherein two subsequent activity counts are used
24 when fitting the curve.
25

26 72. The data storage device of claim 69, wherein the curve is fitted using a numerical
27 method.
28

29 73. The data storage device of claim 72, wherein the numerical method is a least squares fit
30 method.
31

1 74. The data storage device of claim 69, wherein,

2 after receiving an input of the first subsequent activity count, a preliminary patient
3 specific dose is determined; and

4 if the preliminary patient specific dose exceeds a vendor-provided dose, an output is
5 generated warning that an additional vendor-provided dose may be required.

6
7 75. The data storage device of claim 67, wherein the maximum effective mass is determined
8 from a formula of maximum effective mass versus patient height.

9
10 76. The data storage device of claim 75, wherein the activity hour parameter is read from a
11 database of activity hour parameters for particular maximum tolerated doses and particular
12 patient parameters.

13
14 77. The data storage device of claim 75, wherein the initial and subsequent activity counts
15 received by the computer have been corrected to take into account of background radiation prior
16 to being received by the machine

17
18 78. The data storage device of claim 75, wherein the initial and subsequent activity counts
19 received by the machine are corrected to take into account of background radiation after being
20 received by the machine.

21
22 79. The data storage device of claim 78, wherein the correction to take account of
23 background radiation is performed by:

24 receiving an input of a background radiation count; and

25 subtracting the background radiation count from the appropriate activity count.

26
27 80. The data storage device of claim 78, wherein the correction to take account of
28 background radiation is performed by:

29 receiving an input of a plurality of activity counts;

30 receiving an input of a plurality of related background radiation counts;

1 determining a plurality of intermediate corrected activity counts from the activity counts
2 and the related background radiation counts; and
3 determining a corrected activity count as a mean of the intermediate corrected activity
4 counts.

5
6 81. The data storage device of claim 65, wherein doses for less tolerant patients is determined
7 by:

8 displaying categories of less tolerant patients;
9 receiving an input of the selection of a category into which a less tolerant patient falls;
10 and

11 setting a desired total body dose for the particular patient equal to the total body dose for
12 the selected category.

13
14 82. The data storage device of claim 65, wherein patient-specific desired total body doses
15 may be specified by the user of the machine.
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